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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No: 39415-0005

Applicant(s): Sasa KRANJC *et al.*

Confirmation No.: 7627

Serial No.: 09/171,081

Group Art Unit: 1651

Filing Date: December 14, 1998

Examiner: Francisco C. PRATS

Title: PROCESS FOR THE PREPARATION OF CLAVULANIC ACID

DECLARATION OF SASA KRANJC

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Sasa Kranjc, being duly warned, hereby declare and state:

1. I am a Head of Department at Lek Pharmaceuticals. I understand the English language.
2. I have a degree in Microbiology. I am the principal author of numerous scientific articles, and an inventor on U.S. Patent No. 6,365,382. I am a co-inventor on the captioned application. A copy of my *curriculum vitae* is attached (tab F of this Appendix).
3. I have reviewed the office action mailed August 9, 2004 in the captioned application.
4. In the office action mailed August 9, 2004, the Examiner asserts that because the claims under examination are essentially identical or substantially similar to the processes disclosed by Cole *et al.*, the alleged unexpected results must be due to some unclaimed aspect of the process disclosed by the Applicant. The Examiner has alleged that the processes in Applicants' specification contain many parameters and specific strains, none of which are recited

in the claims under examination. The Examiner has further alleged that no step of adding phosphorus is recited in the claims and that the unexpected results are not commensurate in scope with the claims under examination.

5. In support of the response to the Office Action of August 9, 2004, we enclose in the Appendix of this Declaration information to support our argument that the unexpected properties of the claimed invention are not species-specific, but rather, due to the addition of phosphorus to the claimed invention.

- a. Tab A of the Appendix - Descriptions of NaH_2PO_4 and KH_2PO_4
- b. Tab B of the Appendix - Romero J. *et al.*, *Applied Microbiology and Biotechnology*, 20:318 (1984) cited in Office Action response.
- c. Tab C of the Appendix - Lebrihi A. *et al.*, *Applied Microbiology and Biotechnology*, 26:130 (1987) cited in Office Action response.
- d. Tab D of the Appendix - a copy of an additional cultivation experiment of *Streptomyces clavuligerus* ATCC 27064 in which the clavulanic acid yield was similarly high (4,410 $\mu\text{g/ml}$), compared to a yield of 3,580 $\mu\text{g/ml}$ clavulanic acid from the cultivation of *Streptomyces* SP. P 6621 FERM P 2804 in Example 1(B) of the instant specification (*see* page 10 of the specification).
- e. Tab E of the Appendix - ATCC specification sheet for *Streptomyces clavuligerus* NRRL 3585, which is the same as the species *Streptomyces clavuligerus* ATCC 27064. This information proves that other types of *Streptomyces clavuligerus* species also

produce a high level of clavulanic acid, and that the unexpectedly high yield of clavulanic acid in the present invention is not dependent upon what *Streptomyces clavuligerus* species is used.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements and the like are made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

16.11.2004
Date


Sasa KRANJC